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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/351,149	07/12/1999	PHILIP E. THORPE	4001.002383	9329

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EXAMINER
SHARAREH, SHAHNAM J

ART UNIT	PAPER NUMBER
1617	39

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/351,149	Applicant(s) THORPE ET AL.
	Examiner Shahnam Sharareh	Art Unit 1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 43-57* is/are pending in the application.

4a) Of the above claim(s) *10-15,20-23 and 44* is/are withdrawn from consideration.

5)☒ Claim(s) *43* is/are allowed.

6)☒ Claim(s) *1-9,16-19,24-31 and 45-57* is/are rejected.

7)☒ Claim(s) *32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *35,38* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Amendment filed on April 28, 2003 20, 2002, Paper No. 37 has been entered. Claims 1-32, 43-57 are pending.

Claims 10-15, 20-23, 44 are withdrawn from further consideration, as being drawn to a nonelected species. Applicant timely traversed the restriction (election) requirement in Paper No. 15. This application contains claimed 10-15, 20-23, 44 drawn to an invention nonelected with traverse in Paper No. 14. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP. 821.01.

Claim 32 and 43 are free of art.

Applicant's comments regarding which claims are withdrawn or pending on page 15 of the Amendment has been noted. Claims 1-32, 43-57 are pending. Claims 10-15, 20-23, 44 are withdrawn to the extent they are directed to the non-elected species. Office has relied on Applicant's election of species set forth in Paper No. 11, filed on August 21, 2000, which clearly states that claims 10-15, 20-23, 44 are not directed to the species elected. (see Paper No. 11 at page 8). Therefore, said claims were withdrawn from consideration at that point. Inclusion of claim 14 on the anticipation rejection over Schroit was inadvertent and is hereby omitted.

Response to Amendment

Any rejection that is not addressed in this Office Action is considered obviated in view of the Amendments and Arguments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-9, 16-19, 24-31, 45-57 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Schroit US Patent 6,300,308 in view of Gimbrone US Patent 5,632,991, Blackenberg et al US Patent 6,197,278 and Abrams US Patent 4,867,962.

Schroit teaches that various known techniques may be used to prepare more specific antibodies. Schroit elaborates that various types of antibodies such as humanized mAbs, or murine modified antibodies may be used for his methods (see col 4, lines 38-49; col 13, lines 24-55). Schroit, however, fails to specifically disclose the use of other suitable antiphospholipid antibodies in combination with a second anticancer agent conjugated with a targeting antibody.

Gimbrone discloses targeting agents conjugated to an antibody directed to ELAM-1 (E-Selectin), (col 5, lines 18-38). Gimbrone teaches that such endothelial specific adhesion molecules are rapidly unregulated on the surface of cultured human vascular endothelial cells (col 27, lines 59-67). Gimbrone also discloses the use of his targeting agent-therapeutic agent conjugate, alone or in combination with other antibody or antibody fragment and/or a therapeutic agent (a second anti-cancer agent) (col 15, lines 46-55). Therapeutic agents of Gimbrone produce apoptosis as they encompass various toxins, antioxidants and anti-tumor drugs (see col 12-14, claim 2). Finally Gimbrone teaches that E-Selectin or a leukocyte-binding fragment thereof can be coupled to a chemotherapeutic drug that binds to tumor cell expressing receptors for E-Selectin, to kill the tumor cell (col 13, lines 58-67). Gimbrone also disclose methods for

detecting E-Selectin expression within the body of a patient comprising steps of detecting E-Selectin by labeling the E-Selectin antibody with a radioactive isotope that can be detected under a scintillation counter (col 18, lines 60-65). Gimbrone does not teach the combination therapy of his antibody-therapeutic agent conjugate with an anti-aminophospholipids antibody.

Abrams teach that therapeutics conjugates directed to cancer cells comprising a targeting antibody and an active agent is well established in the art (see abstract, col 11-14, claims 1-16).

Blackenberg teaches targeted radiolabeled anaxein V (abstract, col 9, lines 50-55, col 12, lines 33-61, col 20, lines 41-55). Blackenberg does not teach the use of a therapeutic agent

The teachings of Schroit, Gimbrone, Blackenberg, and Abrams, are in the same field of endeavor as they are all directed to the field of antibody immunology.

It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In *re Kerkhoven*, 205 USPQ 1069(CCPA) 1980.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to combine the antiphospholipid antibodies of Schroit with conjugates of Gimbrone or Blackenburg in the same or distinct compositions, because the idea of combining them flows logically from their having been individually taught in prior art. Further, as shown by Abrams, the art of preparing antibody-therapeutic agent construct

to target a specific site is well established in the art. Therefore, the claims that require no more than mixing together two conventional anti-tumor agents set forth prima facie obvious subject matter and as indicated by Abrams, the ordinary skill in the art would have had a reasonable expectation of success in targeting cancerous regions.

Double Patenting

Claims 1-9, 16-19, 24-32, 43, 45-49 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claim of copending Application No. 09/351862. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both directed to kits comprising antibodies directed to aminophospholipids.

Applicants arguments with respect to the provisional double patenting rejection that exists in Sn 09/351,862 have been noted but are not relavent here, because prosecuion of SN 09/351,862 ('862) is separate from the instant application. Applicants further appear to argue that the pending application should contain a double patenting rejection over the co-pending application 09/351,149. In response, Examiner states that the purpose of a provisional double patenting rejection is to place Applicant on proper notice about the overlapping nature of the claimed subject matter. It appears that Applicant has properly been served of such notice to maintain the co-pending claims patentably separate. Nevertheless, to the extent it is relavent, Examiner points out that the claims in this application are generic to the the instant pending claims. The generic claim of this application may not necessarily render the instant species claims obvious.

Accordingly, a one-way obviousess double patenting rejection is made in this application to put Applicant on notice of their burden.

Response to the Arguments

Applicant's arguments with respect to this rejection have been fully considered but they are not persuasive. Applicants improperly attempt to narrow the scope of the claim by reading limitations of the specification into a claim or implicitly adding limitations which have no express basis in the claim. see *In re Morris*, 44 USPQ2d 1023, 1027-28 (Fed.Cir. 1997). With respect to rejection of claims 1, 3-12, 14, 19-22, 39-43 under 35 USC 102 (e) over Schroit US Patent 6,300,308, Examiner states that Applicant's relicance on *Lockheed Martin Corp v. Space Systems/Loral Inc.* 58 USPQ2d 1671 and *In re Cortright*, 49 USPQ2d 1464 is misplaced because the factual scenerios in each of the cited case laws are not applicable in this case.

Lockheed Martin's reasoning is based on improper brodening of a "means plus function" claim which is controlled by 35 USC 112 para 6. The instant claims do not fall under such statutory interpretation of claims. Other cited case laws like *In re Cortright*, are directed to such claim consturction where the prior art applied during the prosecution presented a teaching away from the meaning of the claim as defined in their respective specifications. This is not the case here, because the scope of the claims do not exclude the teachings of the cited references and the cited references do not provide teachings away from the scope of the pending claims. Contrary to Applicant's contention, no where does the instant specification interpret the limitaiton "a

second anti-cancer agent other than the first anti-aminophospholipid antibody or fragments thereof" to exclude such combinations as taught in Schroit.

Applicant essentially argues that the claims at issue ~~are~~ recite the limitation of "a second anti-cancer agent other than the first targeting agent-therapeutic agent constrct." Applicant adds that the first and second construct are two distinct moeities. However, giving the broadest reasonable interpretaion consistent with the specification, the scope of pending claims do not exclude the meaning of two aliquots of the first targeting agent-therapeutic agent. Thus, such limitations are not exclusive of the combinations taught by Schroit because the definitions provided in the instant specification falls within the teachings of Schroit.

Further, the instant Specification at pages 39 sets forth the scope of the limitations "at least first anticancer agents with at least a first antibody....." and "at least a second anti-cancer agent other than said at least a first antibody." At page 39, the specification defines the first limitation described above to be inclusive of Schroit's aminophospholipids. Further, the first at least anticancer agent may be considered to be at least a second anti-cancer agent. (see lines 1-32). Therefore, reading the meaning of such limitations in view of the specification indicates that two separate doses of the first anticancer agent meets the limitations of the instant claims, because the second cancer agent can be the same as the first cancer agent. The antibody-therapeutic conjugates of Schroit is within the scope of the instant limitations, because Schroit teaches anti-PS antibody compositions in a kit form that can be administered seperately (see col 7-8)

and at least each antibody composition of Schroit contains an antibody directed to PS and a polypeptide such as diphtheria toxoid.

Applicant also argues that Schroit's two compositions are the same anticancer agents. The instant claims do not exclude such compositions because as defined in page 39 of the instant specification the first and second anticancer agent are the same. Applicant argues that the present kits are not directed to phosphatidylserine-polypeptide conjugates. However, such conjugates are within the scope of an anticancer agent (see Schroit, claim 21). Finally, the information set forth in Exhibit A was considered but were not found persusive because they are directed to antibodies that are not claimed here.

Applicant argues that diphtheria toxoid of Schroit is a carrier for lipid immunization. In response, Examiner states that regardless of the intended use, diphtheria toxoid of Schroit provides therapeutic activity within the scope of the instant claims. In addition, Gimbrone and Blackenberg provide for a second anticancer agent or therapeutic construct. Therefore, all the limitations of the instant claims are taught.

Finally, the rejection is based on the combination of the teachings set forth in the cited references. Each reference is directed to specific receptor molecule on the surface of human vascular endothelial cells associated with vascularized tumor. Thus, they are viewed to be in the same field of endeavor and are considered combinable. Moreover, the compositions of Schroit, Gimbrone and Blackenberg are used for the same purpose. Accordingly, combining the compositions taught by each reference in order to form third composition that is to be used for very same purpose is *prima facia* obvious. see *In re Kerkhoven*, 205 USPQ 1069(CCPA) 1980. Therefore, claims stand rejected.

Conclusi n

No claims are allowed. Claim 32 is objected because it is based on a rejected claim however, would be allowable if rewritten in independent form.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on May 13, 2003 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone numbers for the organization where this application or proceeding is assigned

are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123

RUSSELL TRAVERS
PRIMARY EXAMINER